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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,791	02/08/2001	Jon A. Wolff	Mirus.006.03	6737
7590	10/26/2004		EXAMINER WOITACH, JOSEPH T	
Mark K. Johnson P.O. Box 510644 New Berlin, WI 53151-0644			ART UNIT	PAPER NUMBER

1632

DATE MAILED: 10/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/779,791

**Applicant(s)**

WOLFF ET AL.

**Examiner**

Joseph T. Voitach

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 June 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                         |                                                                             |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                                |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____                                                             | 6) <input type="checkbox"/> Other: _____                                    |

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 21, 2004 has been entered.

**DETAILED ACTION**

This application filed February 8, 2001, is a continuation in part of application 09/312,351, filed May 14, 1999.

Applicants' amendment filed June 10, 2004 has been received and entered. The specification has been amended. Claims 1, 2, 6 and 13 have been amended. Claims 7-12 have been canceled. Claims 1-6 and 13 are pending and currently under examination.

***Election/Restriction***

As noted in the previous office actions, Groups I and II (claims 1-6 and 13) had been rejoined. Applicant timely traversed the restriction (election) requirement in Paper No. 15. Claims 1-6 and 13 are currently under examination as they are drawn to a compound for inserting into an organism comprising (a) a disulfide bond which is cleaved more rapidly than oxidized glutathione and which one of the constituent thiols has a lower pKa than glutathione and (b) a transduction signal wherein the signal is a polymer containing a cationic charge.

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Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Priority***

The amendment to the specification and the petition filed under 37 CFR 1.78 have been received.

As noted previously, this application contains subject matter disclosed in prior Application No. 60/085,764, filed May 16, 1998. The amendment to the specification has established the priority claim to May 16, 1998.

### ***Claim Objections***

Claim 6 objected to because claim 6 recites the “compound of claim 5 claim 1 wherein the transduction signal...” is withdrawn.

Amendment to the claim has obviated the basis of the objection.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-6 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, the recitation of "enhances delivery of said molecule to the cytoplasm of sad cell" is considered new matter. Applicants have not pointed to the specification for support of the amendment, and upon review of the specification Examiner can not find literal support for this amendment. It is noted the "transduction signals" is generally defined to transport themselves across membranes (bottom of page 25), however this does not support enhanced delivery to the cytoplasm. It is noted that the working examples appear to have tested specific sequences with cells in culture but the specific results are not provided in the disclosure. While example 10, is noted as support, the description of the results only indicate that the fluorescence could be detected inside the cell and does not indicate clearly that is in reference to the cytoplasm or the entire cell. More importantly, a review of the relevant art indicates that sequences such as VP22 do not necessarily enhance nor uniquely result in deposition of a compound in the cytoplasm. For example, Normand *et al.* (JBC, 2001) clearly demonstrate that oligonucleotides linked to VP22 accumulate in the nuclei (bridging first and second columns, page 15042, and top of first column, page 15048).

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 1-6 and 13 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

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one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. As discussed above, Normand *et al.* demonstrate that the function of VP22, one of the specifically claimed species does not result in enhancing delivery to the cytoplasm clearly demonstrating that empirical nature of testing each particular composition encompassed by the claims to determine if each structure meets the functional limitations set forth in the claims.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure" (emphasis added).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-6, 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, newly amended claim 1 is indefinite in the recitation of "mammalian physiological conditions". The specification provides no specific definition of the conditions encompassed by this term nor methods and guidance for determining what these conditions encompass. It is noted that the specification supports the intended use of the compound in a mammal, however it fails to provide support for what physiological conditions exist in a mammal. Further, since physiological conditions can vary widely within even a single mammal, for example between cells in the stomach and the brain, the claim is indefinite because it is dependent on the physiological condition one chooses to use in determining the metes and bounds of the claim. Dependent claims 2-6 and 13 are included in the basis of the rejection because they fail to further clarify the nature of the physiological condition and only further define the compounds attached to the product.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects

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for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(f) he did not himself invent the subject matter sought to be patented.

Claims 1, 5 and 6 rejected under 35 U.S.C. 102(a) as being anticipated by Bulaj *et al.*

(IDS reference) as evidenced by Szajewski *et al.* (IDS reference) is withdrawn.

Claims 1 and 5 rejected under 35 U.S.C. 102(b) as being anticipated by Keire *et al.* (IDS reference) is withdrawn.

Claims 1, 2, 5, 6 and 13 rejected under 35 U.S.C. 102(e) as being anticipated by Stein *et al.* (6,258,774 B1) is withdrawn.

The amendments to the claims to encompass specific functional limitations associated with the specific structural features has differentiated the claimed compounds from that disclosed in Bulaj *et al.*, Keire *et al.* and Stein *et al.* Therefore, the rejections are is withdrawn.

Claims 1, 5, 6 and 13 rejected under 35 U.S.C. 102(e) as being anticipated by Monahan *et al.* (6,429,200B1) is withdrawn.

The amendment to change the priority information has obviated the rejection.

Claims 1-6 and 13 stand rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Applicants do not specifically address the basis of the 102(f) rejection in the instant amendment, therefore the rejection is maintained for the reasons of record. Specifically, it is not

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clear why the inventors on each of the patent and the application are not the same. The claim for priority is noted, however this does not determine why the inventorship is different.

As set forth in the previous office actions, US Patent 6,429,200 B1 provides the same general guidance for the chemical linkage of conjugates through disulfide bonds set forth in the instant claims (see for example column 8, lines 5-28). Further, '200 contemplates conjugating gene transfer enhancing agents (column 11, lines 14-21) such as compounds and peptides which aid in the uptake of the compound conjugates. In dependent claim 8 specifically recites that the claimed complexes and process of using contain a disulfide bond (column 24). Upon review of the specification the only teaching for any specific form of a disulfide bond is found at column 8, lines 5-28, which is the same as instantly claimed. Upon review both the instant application and '200 have claims encompassing products containing disulfide bonds and methods of use which are the same.

### ***Conclusion***

No claim is allowed. The claims are free of the art of record because the art fails to teach compounds with the structural and functional properties of those instantly claimed. However, the claims are subject other rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Weitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Voitach

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